OL. XI, No. 8 NOVEMBER, 1950

10.5
873

JAN 3 1951

BORDEN'S REVIEW

of

NUTRITION RESEARCH

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BORDEN'S REVIEW
of
NUTRITION RESEARCH

Reviews and summaries of research information concerning nutrition and foods. Published monthly, except July and August, by THE BORDEN COMPANY; officers of the Company: Theodore G. Montague, president; E. L. Noetzel, treasurer; T. D. Waibel, secretary. Editorial office: 350 Madison Avenue, New York 17, N. Y.

DYNAMIC INTERRELATIONSHIPS IN AMINO ACID NUTRITION

By RUTH WOODS

The development of the concept of the essential nature of certain amino acids, in contrast to the relative dispensability of others, with respect to dietary requirements, has been one of the major milestones of nutrition research. Although the fundamental importance of the proteins in nutrition was foreshadowed by the researches of Magendie and Mulder more than one hundred years ago, it was not until chemists discovered the complex nature of the protein molecule in terms of the amino acid components that the relationship between amino acid composition and variations in the nutritive quality of proteins from various sources became apparent. From this point on, it was realized that basic knowledge of protein nutrition could be attained only through an understanding of the behavior and biological role of the individual amino acids. This realization found fruition in the pioneer studies of Hopkins at Cambridge, Osborne and Mendel at Yale and many other early investigators and reached a climax in the classic studies of Rose and coworkers at the University of Illinois with the development of the concept of essential amino acids.*

The concept of the dietary essentiality of certain amino acids has formed the basis of many important advances in the newer knowledge of protein nutrition. It has, for example, made possible the estimation of protein value on the basis of chemical estimation of their essential amino acid content; it has led to the classification of proteins as complete or incomplete with the important corollary of protein supplementation as a means of improving the protein value of diets†; it has led to the development of the time factor as a primary function in the phenomenon of supplementation.

Perhaps one of the most intriguing aspects of nutrition research in general is the rapidity of its development and the constantly changing facets of basic precepts which are revealed by current progress in this ever new, still young science. With the unfolding of new knowledge, old concepts and principles must be continually viewed anew, reinterpreted and, frequently revised. There is scarcely any phase of nutrition research of which this is not true, as for example: the etiology of pellagra, the interrelations between iodine and thyroid function, the nature of the transmethylation process, to cite a few. Nor has the time-honored concept of essential amino acids

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*cf. *Borden's Review of Nutrition Research,* January, 1945, "The Amino Acids in Nutrition."
†cf. *Borden's Review of Nutrition Research,* May, 1950, "The Utilization of Dietary Protein."

escaped the influence of what one might term the "nutrition revolution." While still fundamentally true, the original concept of essential and non-essential amino acids must now be reviewed in the light of very recent researches which highlight the newly found significance of the so-called "non-essential" amino acids and their close interplay with the "essential" group. As the dynamic aspects of intermediate metabolism in all of its phases become increasingly apparent, the demarcation between essential and non-essential amino acids gradually vanishes, so that one might be led eventually to classify the amino acids not as absolutely essential or not, but rather as to the varying *degree* to which each one of the twenty-three now known may be dispensed with in the diet.

The Concept of Essential Amino Acids:

The concept of the essential amino acids grew out of the early chemical studies on proteins which showed that these substances are composed of amino acids and that, moreover, each specific protein has its own characteristic amino acid makeup which differentiates it from other proteins. This knowledge paved the way toward a clearer understanding of the fact that not all proteins are of equal nutritive value. That this fact is dependent on amino acid composition was demonstrated, some fifty years ago, by Hopkins *et al* (1, 2). They isolated the amino acid, tryptophan, and showed that some proteins (such as zein, from corn) contained no tryptophan and failed to support life in mice unless tryptophan was added to the diet. Other workers, notably Osborne and Mendel, extended these studies to other proteins and amino acids and were able to demonstrate thereby the necessity of other amino acids such as lysine, cystine, arginine, histidine, etc. for proper growth or for maintenance of life in rats. They pointed out (3) that *"the relative values of the different proteins in nutrition are based upon their content of those special amino acids which cannot be synthesized in the animal body and which are indispensable for certain distinct, as not yet clearly defined, processes which we express as maintenance or repair."*

Osborne and Mendel clearly recognized that although some amino acids were required in the diet, while others could be synthesized in the body, *most — if not all — of the amino acids are indispensable for the construction of body tissue* and, therefore, for life and growth.* Modern analytical methods clearly reveal the presence in animal tissue proteins of all of the 23 known amino acids. This confirms the observation that all are indeed essential in animal protein synthesis, since the final protein product cannot be made in the absence of any one constituent amino acid.

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*Also, as we now know, for manufacture of hormones, enzymes, etc.

†*cf. Borden's Review of Nutrition Research,* January, 1945, "The Amino Acids in Nutrition."

Some confusion has developed concerning the meaning or use of the terms "essential" and "non-essential" amino acids. This has resulted from a lack of clarity concerning the definitions of these terms as developed by various investigators. Furthermore, the classification of amino acids into these two groups is meaningful only with respect to the criteria of evaluation used and the particular animal species studied.

Definition of Essential Amino Acids:

According to the early studies, any amino acid whose absence *in the diet* resulted in growth failure or death was classified as essential. Using growth of rats as the criterion and working with mixtures of purified amino acids, a classification of the 23 amino acids into essential and non-essential was worked out by Rose *et al* (4) after many years of painstaking research.†

On this basis, Rose and colleagues stated that ten amino acids are required *in the diet of the rat for optimum growth* and that the remaining thirteen may be omitted from the diet inasmuch as they are probably synthesized in adequate amounts at rates commensurate with the demands for normal growth (Table 1).

Table 1. Final classification of the amino acids with respect to their growth effects in experimental animals.

Indispensable	*Dispensable*
Lysine	Glycine
Tryptophan	Alanine
Histidine	Serine
Phenylalanine	Norleucine
Leucine	Aspartic acid
Isoleucine	Glutamic acid
Threonine	Hydroxyglutamic acid
Methionine	Proline
Valine	Hydroxyproline
*Arginine	Citrulline
	Tyrosine
	Cystine

*Arginine can be synthesized by the animal organism, but not at a sufficiently rapid rate to meet the demands of normal growth.

Requirements for Essential Amino Acids: In addition to *qualitatively* classifying the ten amino acids listed in Table 1 as dietary essentials, Rose *et al* established quantitative requirements for each of these for the growing rat under their specific experimental conditions.

In studies by other investigators, classification of amino acids as dietary essentials was made according to the use of many other criteria. These have included the role of amino acids in supporting body maintenance (as determined by weight gains or nitrogen balance); in permitting the regeneration of blood plasma proteins in experimentally depleted animals; in establishing successful lactation in adult female animals, etc. Even using the same criteria, however, findings will differ according to the test animal used (rat, mouse, chick, dog, man), a fact which was not appreciated in many of the early studies.

Variations in Findings with Respect to Differences in Criteria and Species Studied: Using the immature, growing rat as the test animal and with optimum growth as the goal, it has been shown that arginine is a dietary essential for the rat. Using the adult, full-grown rat as the test animal and maintenance of body weight as the criterion of essentiality, it has been found that arginine is not needed by the rat. This variation in the role of arginine in the same species is explained by Rose by assuming that arginine is synthesized in the rat at a rate sufficient for the lesser needs of body maintenance, but too slowly to meet the more excessive needs for the building of new tissue (i.e. new protein synthesis) which is characteristic of rapid growth.

Similarly, using the growing rat as the experimental medium, glycine has been shown to be a dietary non-essential. When the growing chick is used as the test animal, glycine becomes a critically needed dietary essential (5). In the chick, therefore, there is a limited ability to synthesize glycine and the status of this amino acid changes from non-essential to essential. It is of interest to note that the need for glycine increases in more rapidly feathering breeds of chickens since feather protein contains large amounts of glycine. Thus, even in the same species (chick) the degree of essentiality of glycine may vary. In contrast to the growing rat, the young chick needs not ten amino acids but twelve, and under certain special conditions, fourteen (Table 2).

Furthermore, within the last three years, evidence has developed which indicates that even using the same species (rat) and the same criterion (rate of growth), the ten amino acids enumerated as dietary essentials more than ten years ago by Rose can no longer be regarded as a complete mixture for best growth in the rat. This has been traced to the entirely new conditions prevailing with the use of the new, improved basal diets which have recently become available as a result of modern research in nutrition.

Table 2. Dietary Amino Acid Requirements for Normal Growth of Chicks (5)

May be absent without detriment to growth:	Required under certain conditions:	Required for normal growth:
Alanine	Cystine	Arginine
Aspartic Acid	Tyrosine	Glutamic Acid
Hydroxyproline		Glycine
Proline		Histidine
Serine		Isoleucine
		Leucine
		Lysine
		Methionine
		Phenylalanine
		Threonine
		Tryptophan
		Valine

Importance of the "Non-Essential" Amino Acids:

For Growth: In a paper published during 1948, Rose *et al* (6) point out that in their experiments of ten years ago the ten essential amino acids when fed as the sole source of dietary nitrogen produced growth in rats comparable to that obtained with an intact protein, such as casein. During the ten years that followed this work, however, new information was acquired concerning the nutritive needs of the rat, new vitamins were discovered and became available in crystalline form for experimental use and, as a result, basal diets were changed radically. The improvement in basal diets made apparent certain deficiencies which had hitherto been undetected and also established a new criterion for optimum growth in the rat.

Accordingly, with the newer knowledge of rat nutrition and the higher standards for growth progress, Rose *et al* found that a mixture of the original ten amino acids gives a rate of growth which is only about 70-75% as much as is obtained on a mixture of nineteen amino acids. These findings indicate that there is a need for some of the "non-essential" amino acids, whose synthesis apparently cannot keep pace with the requirements of very rapid growth.

These findings were confirmed by Russell and Taylor (7). They reported that a mixture of the ten essential amino acids plus low levels of casein giving a combined total of essential amino acids equalling the minimal amounts suggested by Rose, gave superior growth to a mixture containing the same quality of the ten amino acids alone. Further, an increase in the quantity of essential nitrogen (supplied by increased amounts of the essential amino acids alone) designed to equal the total nitrogen (essential and non-essential) provided by the low casein-essential amino acid mixture,

failed to cause a significantly greater gain than that observed with minimum levels of the essential amino acids alone. Thus, a specific need for some nitrogen in the form of the non-essential amino acids was shown. Ramasarma *et al* (8) similarly demonstrated a need for the non-essential amino acids and postulate that the conversion of some of the essential to the non-essentials in the body may not be sufficient to provide adequate amounts of both as rapidly as body needs require them. The nature of the ration as a whole, furthermore, may influence the rate of these conversions and syntheses, they suggest, but these speculations can not yet be accepted until further data are available. Ramasarma *et al* also point out the possibility that the inferior growth with mixtures of 18 amino acids as compared to growth on intact casein may be due to the presence of unnatural isomers of the amino acids used to provide non-essential nitrogen. Such isomers may not be fully utilized by certain animals.

(Other Species): The need for a supply of "non-essential" nitrogen in addition to the basic essentials extends to other species, as for example, the mouse (9, 10) and the dog (11). Various sources of nitrogen have been shown to provide the required "non-essential" nitrogen for growth. Thus the dietary addition of *single* amino acids (6, 8, 9), of mixtures containing only a few of the non-essential amino acids (8, 9), urea (12) or even ammonium salts (12, 13) may increase the growth-promoting properties of the essential amino acids for rodents. The rat is able to use ammonium salts for this purpose (12, 13), but the mouse can do so only to a limited extent (9).

Tyrosine (8) and proline (14), two non-essential amino acids, have been shown under certain conditions to stimulate growth in the rat. In the mouse (9), glutamic acid (a non-essential) was found to supplement a mixture of essential amino acids. Further, part of the glutamic acid supplement was shown to be replaceable by a mixture of DL-serine, DL-alanine, L-tyrosine and DL-asparagine which similarly enhanced growth. Again in rats, Rose *et al* (6) found glutamic acid (a non-essential) markedly stimulatory to rat growth when only the ten essentials were provided; when, however, glutamic acid was removed from a more adequate mixture of 19 amino acids, no appreciable growth depression due to its absence was noted.

Further relationships between the essential and non-essential amino acids have been revealed by the newer studies of Rose's group (6). They report, for example, that the non-essential* cystine can replace about one-sixth of the essential methionine requirement — but only when methionine is in the diet. In the absence of dietary methionine, cystine has no growth effect. This

*For growth in the rat.

may indicate a sparing action of cystine for methionine. In other words, some of the dietary methionine is used by the body as such and some of it is used in the body synthesis of cystine. If, however, cystine is supplied pre-formed in the diet, the amount of methionine ordinarily used for its synthesis may be deducted from the dietary requirement. Rose *et al* found, similarly, that about half of the phenylalanine requirement may be replaced by the non-essential tyrosine. Again, however, in the complete dietary absence of phenylalanine, tyrosine has no growth properties. In the same manner, glutamic acid and also proline can each replace arginine to a slight degree. However, providing extra amounts of the essentials still does not obviate the growth-stimulating properties of the non-essentials, as shown by the work of Russell and Taylor (7).

On the basis of their newer findings, Rose, Oesterling and Womack suggest the following modified classification of amino acids based only on the needs of the young rat for growth (Table 3).

Table 3. Classification of Amino Acids with Respect to their Growth Effect in the Rat (6)

Essential	*Non-Essential*
Lysine	Glycine
Tryptophan	Alanine
Histidine	Serine
Phenylalanine	Cystine*
Leucine	Tyrosine†
Isoleucine	Aspartic Acid
Threonine	Glutamic Acid‡
Methionine	Proline‡
Valine	Hydroxyproline
Arginine§	Citrulline

*Cystine can replace about 1/6 of the methionine requirement, but has no growth effect in the *absence* of methionine.

†Tyrosine can replace about 1/2 of the phenylalanine requirement, but has no growth effect in the *absence* of phenylalanine.

‡Glutamic acid and proline can serve individually as rather ineffective substitutes for arginine in the diet. This property is not shared by hydroxyproline.

§Arginine can be synthesized by the rat, but not at a sufficiently rapid rate to meet the demands of *maximum* growth. Its classification, therefore, as essential or non-essential is purely a matter of definition.

For Maintenance: In an extremely detailed series of studies with rats, Cannon *et al* have estimated both the qualitative (15) and quantitative requirements of adult rats for the essential amino acids. Using "maintenance" as their criterion, they defined this term as "maintenance of health as evidenced by the preservation of weight and appetite as well as nitrogen balance." They demonstrated that under the conditions of their tests, adult rats

do not need a source of nitrogen other than nine of the ten amino acids considered essential for growth in the young rat.* Under these circumstances, the borderline amino acid, arginine, was classified as non-essential.

Other studies by Swanson and colleagues (17), however, have shown that under their conditions the well-nourished rat does not have the capacity to synthesize the non-essential amino acids at a rate that will meet the needs of body maintenance as measured by nitrogen balance.

Using nitrogen balance as the criterion of maintenance, Rose and co-workers determined over a period of seven years, both the qualitative (18) and quantitative (19) amino acid requirements in adult man. Subjects were kept on synthetic diets of purified amino acids, sugar, butter, starch, and vitamins. Of the total nitrogen content of the diet (7-10 gm.) only about 0.35 gm. represented nitrogen of an unknown nature. Nitrogen balance was maintained when only eight of the ten amino acids essential for growth in the rat were supplied. Arginine and histidine were found not to be needed in the diet for maintenance in the human male adult. By gradually lowering the amount of one of the eight amino acids until a negative nitrogen balance was reached, a tentative figure for the minimum amount of each one of these in turn was reached. In these experiments, however, glycine and urea were furnished in order to supply the nitrogen for the synthesis of the non-essential amino acids. Table 4 summarizes these findings:

Table 4. Minimum and Recommended Intakes for Normal Man when Diet Furnishes Sufficient Nitrogen for Synthesis of Non-Essentials (19)
(Strictly Tentative Values)

Table 4a.

Amino Acid	Minimum Daily Requirement	Recommended Daily Intake	Amino Acids in Milk
	gm.	gm.	gms. per qt.
L-Tryptophan	0.25	0.5	0.5
L-Phenylalanine	1.10	2.2	1.9
L-Lysine	0.80	1.6	2.6
L-Threonine	0.50	1.0	1.6
L-Valine	0.80	1.6	2.3
L-Methionine	1.10	2.2	1.1
L-Leucine	1.10	2.2	3.9
L-Isoleucine	0.70	1.4	2.1

When these values have been confirmed, they will offer for the first time a practical means of evaluating dietary proteins in terms of their ability to

*Other workers, employing different experimental conditions, have reported the need for only five of the basic "essential" amino acids (16).

maintain adults in nitrogen balance. As an example, the value of milk as a biologically complete protein has often been stressed by nutritionists. Table 4a shows how this concept bears critical investigation by a comparison of the amino acid values of milk with the tentative human requirements.

For Repletion: The essential amino acids required for the repletion of body tissue in starved rats have been determined both qualitatively and quantitatively by Steffee *et al* (20). The authors point out that the values obtained have no absolute meaning except under the experimental conditions used, but they believe that the proportions of the amino acids required in relation to each other may be significant.

In repletion, as in growth, non-essential amino acids must be provided in the diet for best results. In studies by Frost (21, 22) it was found that optimum repletion took place when 20 to 25% of the total dietary nitrogen was provided in the form of the non-essential amino acids.

Dynamic Aspects of Essential and Non-Essential Amino Acids:

The newer findings with respect to the need for "non-essential" amino acids in the diet are further evidence of the intricate, delicately balanced dynamic equilibrium which exists among the body constituents, including dietary components. The classical isotope experiments of Schoenheimer's group (23)* showed that when a specific quantity of an amino acid (either "essential" or "non-essential") is fed, part of this quantity is excreted, part incorporated unchanged into tissue protein, and still another portion enters into the so-called metabolic pool where it undergoes degradation, resynthesis and recombination into other amino acids and, eventually, into new protein.

Some of the dietary essential amino acids can be synthesized in the body with respect to both the carbon chain and nitrogen moieties. Others, such as leucine and histidine, are indispensable in that the carbon chain is difficult to synthesize; the amino group, however, can be readily derived from some other physiological compound. An outstanding exception is the amino acid, *lysine,* which is not involved in reversible reactions in either the nitrogen or carbon fractions. It is thus regarded as a single, indispensable chemical unit which has to be supplied to the body intact and pre-formed.

These experiments, as well as those described earlier in this Review, emphasize the importance of the concept of *relative rate of synthesis* rather

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**cf. Borden's Review of Nutrition Research,* "Isotopes in Nutrition Research I. The Intermediate Metabolism of Fats, Proteins and Carbohydrates," October, 1945.

than of absolute dispensability or indispensability as the determining factor in establishing amino acid requirements.*

The effect of this complex interplay of biochemical factors is clearly apparent in the confusion, which is only now being clarified, with respect to the interpretation of amino acid requirements. The need for a single nutritional factor cannot, as was once thought, be defined in simple, unqualified terms. Requirements are influenced by many interdependent factors: the general health of the body; the synthesizing capacity of the liver and other specialized organs; the overall composition of the diet; the nature of the reserve storage materials; the efficiency of existing enzyme systems governing biological degradations and syntheses; and numerous other constantly fluctuating conditions. Not only is it almost impossible to define quantitative needs for each of the amino acids (except under very specific conditions) but it is becoming questionable as to where one may draw the line — if at all — between those amino acids which are essential in the diet and those which are not.

From a nutritional standpoint, these studies emphasize the desirability of providing in the diet ample supplies of all the amino acids either by the use of complete protein foods such as meat, eggs, milk, fish, cheese and the like, or by using mutually supplementary combinations of protein foods.

*An interesting thought arising from this concept is the possibility that the increased dietary needs for the essential amino acids in the immature, growing animal may be due not merely to the increased demands associated with synthesis of new tissue, but also to the relative inadequacy of the as yet incomplete enzyme systems involved in the processes of amino acid and protein synthesis (24).

REFERENCES CITED

1. HOPKINS, F. G. and S. W. Cole. Proc. Roy. Soc. *68,* 21 (1901).

2. WILLCOCK, E. G. and F. G. Hopkins. The importance of individual amino acids in metabolism: observations on the effect of adding tryptophane to a dietary in which zein is the sole nitrogenous constituent. *J. Physiol. 35,* 88 (1906).

3. OSBORNE, T. B. and L. B. Mendel. Amino acids in nutrition and growth. *J. Biol. Chem. 17,* 325 (1914).

4. ROSE, W. C. The nutritive significance of the amino acids. *Physiol. Rev. 18,* 109 (1938).

5. ALMQUIST, H. J. The amino acid requirements of avian species, in *Proteins and Amino Acids in Nutrition,* ed. by M. Sahyun, p. 221, Reinhold Pub. Corp., N. Y. (1948).

6. ROSE, W. C., M. J. Oesterling and M. Womack. Comparative growth on diets containing ten and nineteen amino acids with further observations on the role of glutamic and aspartic acids. *J. Biol. Chem. 176,* 753 (1948).

7. RUSSELL, W. C. and M. W. Taylor. Growth efficiency of essential amino acids alone and in combination with casein. *J. Nutr. 36,* 751 (1948).

8. RAMASARMA, G. B., L. M. Henderson and C. A. Elvehjem. Purified amino acids as a source of nitrogen for the growing rat. *J. Nutr. 38,* 177 (1949).

9. MADDY, K. H. and C. A. Elvehjem. Studies on growth of mice fed rations containing free amino acids. *J. Biol. Chem. 177,* 577 (1949).

10. BRAND, E. and D. K. Bosshardt. Abstr. Am. Chem. Soc., 114th Meeting, Washington, D. C. Sept. (1948).

11. SILBER, R. H., E. E. Howe, C. C. Porter and C. W. Mushett. Growth and maintenance of dogs fed amino acids as the source of dietary nitrogen. *J. Nutr. 37,* 429 (1949).

12. ROSE, W. C., L. C. Smith, M. Womack and M. Shane. The utilization of the nitrogen of ammonium salts, urea and certain other compounds in the synthesis of non-essential amino acids in vivo. *J. Biol. Chem. 181,* 307 (1949).

13. LARDY, H. A. and G. Feldott. The utilization of ammonium nitrogen by the growing rat. *J. Biol. Chem. 179,* 509 (1949).

14. WOMACK, M. and W. C. Rose. The role of proline, hydroxyproline and glutamic acid in growth. *J. Biol. Chem. 171,* 37 (1947).

15. WISSLER, R. W., C. H. Steffee, L. E. Frazier, R. L. Woolridge and E. P. Benditt. Studies in amino acid utilization. III. The role of the indispensable amino acids in maintenance of the adult albino rat. *J. Nutr. 36,* 245 (1948).

16. BURROUGHS, E. W., H. S. Burroughs and H. H. Mitchell. The amino acids required for the complete replacement of endogenous losses in the rat. *J. Nutr. 19,* 363 (1940).

17. SWANSON, P. P. and H. E. Clark. The metabolism of proteins and amino acids. *Ann. Rev. Biochem. 19,* 235 (1950).

18. ROSE, W. C. The role of the amino acids in human nutrition. *Proc. Am. Phil. Soc. 91,* 112 (1947).

19. ROSE, W. C. Human amino acid requirements. *Fed. Proc. 8,* 546 (1949).

20. STEFFEE, C. H., R. W. Wissler, E. M. Humphreys, E. P. Benditt, R. L. Woolridge and P. R. Cannon. Studies in amino acid utilization V. The determination of minimum daily essential amino acid requirements in protein-depleted adult male albino rats. *J. Nutr. 40,* 483 (1950).

21. FROST, D. V. and H. R. Sandy. Rat repletion studies with amino acid solutions. Role of non-essential amino acids. *Fed. Proc. 8,* 383 (1949).

22. FROST, D. V. Abstracts Am. Chem. Soc., 116th meeting, Atlantic City, Sept. (1949).

23. SCHOENHEIMER, R. *Dynamic State of Body Constituents,* Princeton Univ. Press (1942).

24. ADLER, E. Personal Communication (1950).

NEWS DIGEST

BREAKFAST HABITS: An experiment involving 10 women was performed to show the effects of various breakfast patterns on physiologic response. The subjects lived in a university dormitory and ate all their meals in the hospital dining room supervised by the nutrition department. The breakfast patterns used were: (1) basic breakfast representing approximately one-fourth the total daily caloric requirement (600 cal.); (2) light breakfast (270 cal.); (3) heavy breakfast (1000 cal.); and (4) no breakfast. Responses studied were (1) neuromuscular tremor magnitude, (2) capacity to do work, (3) choice reaction time, and (4) strength endurance. Each breakfast pattern lasted 5 weeks. Comparison of data collected twice weekly for each breakfast pattern justified the following conclusions: No differentiation by way of tremor magnitude, capacity to do work, choice reaction time or strength endurance could be established following regular consumption of heavy and light breakfasts respectively, of ordinary breakfast items. In comparison with omission of breakfast, consumption of a 600 cal. breakfast consisting of fruit, cereal, milk, sugar, toast and butter resulted in a significant reduction of tremor magnitude in all cases and an increase in maximum work output in 80% of the cases during the period when food was consumed at breakfast time. Strength endurance was unaffected.—*Fed. Proc. 9,* 127 (1950).

PHENYLALANINE REQUIREMENTS OF CHILDREN: The available data on the amino acid requirements of man have been secured for the most part by the depletion procedure. The difference between the repletion needs so obtained and normal maintenance values increases with the duration of the depletion period which is known to involve numerous biochemical readjustments. In order to obtain amino acid requirement data which will have both practical and fundamental applications, means have been explored whereby measurements of the physiological availability of amino acids can be made under optimal dietary conditions as they prevail in life. This involves a determination of the "saturation point" of a test amino acid which is added stepwise to the diet of subjects maintained in normal N-metabolism by natural foods fed *ad libitum*. Preliminary observations by the use of this technique show that when evaporated milk constitutes the principal source of dietary protein, the phenylalanine saturation point is reached when the diet contains 170 mg. of *l*-phenylalanine per kilo per day for 6 to 8 month old children. The saturation level for 3-month old children is reached sharply at 205 mg. of *l*-phenylalanine. Calculations from these figures disclose that the normal phenylalanine needs of infants can be met by evaporated milk formulae which provide 4.2 gm. of milk protein per kilo per day for the first three months of life and 3.6 gm. of milk proteins for the last six months of the first year of life. —*Fed. Proc. 9,* 144 (1950).